

## REMARKS

Applicants would like to thank Examiners Bowman and Schultz for the telephonic interview granted on October 17, 2006 to Applicants' representative Frances Putkey.

Following entry of the amendments submitted herewith, claims 8, 14-17, 25, 30, 32, 52-56, and 59-71 will be pending in the instant application. Claims 1-7, 9-13, 18-24, 26-29, 31, 33-51, and 57-58 are canceled without prejudice or disclaimer. Applicants reserve their right to pursue the subject matter of these claims in one or more continuing applications.

Claims 8, 14-17, 25, 30, 32, 52-56 and 59 are currently amended. Claims 61-71 are newly introduced. No new matter is added by way of these amendments, as support for the claim amendments and newly introduced claims is found throughout the specification as filed. For example, support for antisense oligonucleotides comprising at least 8 consecutive nucleobases of SEQ ID NO: 23 and 100% complementary to SEQ ID NO: 4 is found at page 9, lines 16-18, at page 14, lines 23-27, and in Table 1; support for selecting a human having elevated serum lipoprotein(a) levels is found at page 3, lines 19-26; support for chimeric antisense oligonucleotides, as recited in claims 60-62 and 65-67, is found at page 59, lines 18-23 and at page 80 lines 12-20. Support for newly added claims 70 and 71 is found in Example 15, which illustrates SEQ ID NO: 23 having the chemical modifications recited in claims 70 and 71.

Each of claims 8, 14-17, 25, 30, 32, 52-56 and 59 are amended in response to a formalities objection. Additionally, claims 8, 52, and 59 are amended for clarity.

Applicants note that claims 41-44 and 46-49 were withdrawn by the Examiner. As stated above, Applicants have canceled claims 41-44 and 46-49, without prejudice to pursuing the subject matter of these claims in a continuing application.

Each of the currently pending claims is fully supported by the specification as originally filed as well as the documents to which the instant application claims priority. As such, the instant application contains no new matter.

## Response to Arguments-Claim Rejections

*35 U.S.C. §102*

**Claims 6, 7, 14, 25, 30, and 32** are rejected under 35 U.S.C § 102(b) as allegedly being anticipated by Rouy et al. The Examiner asserts that Rouy et al. teach a method comprising administering an apolipoprotein(a) antisense oligonucleotide to a cell or tissue and teach that

such antisense nucleic acids are capable of specifically hybridizing with a nucleic acid encoding apolipoprotein(a) such that down regulation of the target gene expression can be achieved. Claims 6 and 7 are canceled, rendering the rejection of these claims moot, thus the rejection will be addressed as it relates to claims 14, 25, 30, and 32.

While Applicants disagree that Rouy et al. teach the methods as instantly claimed, solely in the interest of advancing prosecution, independent claims 25 and 30 have been amended to recite administration of an antisense oligonucleotide comprising at least 8 contiguous nucleobases of SEQ ID NO: 23 that is 100% complementary to SEQ ID NO: 4. Rouy et al. do not teach a method comprising administering an antisense oligonucleotide comprising at least 8 contiguous nucleobases of SEQ ID NO: 23 that is 100% complementary to SEQ ID NO: 4. Because claim 14 depends from claim 25 and claim 32 depends from claim 30, Rouy et al. do not anticipate any of these claims.

In view of the foregoing amendments and remarks, Applicants request that the rejection of claims 14, 25, 30 and 32 be withdrawn.

*35 U.S.C. §103*

**Claims 6-8, 14-17, 22, and 25** are rejected under 35 U.S.C § 103(a) as allegedly being unpatentable over Morishita et al., in view of Frank et al., and further in view of Baracchini et al. Applicants respectfully disagree. Claims 6, 7, and 22 have been canceled, rendering the rejection of these claims moot. Thus, the rejection will be addressed with respect to pending claims 8, 14-17, and 25.

While Applicants disagree with the Examiner's conclusion that it would have been obvious to target apolipoprotein(a) with antisense oligonucleotides in view of Morishita et al., Frank et al., and Baracchini et al., solely in an effort to advance prosecution, claim 25 has been amended to recite an antisense oligonucleotide comprising "at least 8 consecutive nucleobases of SEQ ID NO: 23." The combination of Morishita et al., Frank et al., and Baracchini et al. do not teach or suggest all of the limitations of amended claim 25, or any claim depending therefrom. Accordingly, Applicants submit the Examiner's rejection fails to establish a prima facie case of obviousness and Applicants request that the rejection of claims 8, 14-17, and 25 be withdrawn.

*Double Patenting*

The Examiner notes Applicants' request to defer addressing the obviousness-type double patenting rejection of Claims 6-8, 14-17, 22, 25, 30, and 32 in view of copending application 10/485,113. Applicants bring to the Examiner's attention that U.S. Application No. 10/485,113 is no longer pending, and request that the obviousness-type double patenting rejection in view of this application be withdrawn.

The Examiner additionally notes Applicants' request to defer addressing the obviousness-type double patenting rejection of claims 6-8, 14-17, 22, and 25 in view of copending U.S. Application No. 09/923,515, until such time as the claims are otherwise in condition for allowance.

**New Rejections/Objections**

*Claim Objections*

**Claims 6-8, 14-17, 22, 25, 30, 32, 40, 45, and 50-59** are objected to because none of the claims has a period after the claim number. As requested by the Examiner, Applicants have corrected this informality for claims that have not been canceled. As such, Applicants respectfully request that this objection be withdrawn.

*35 U.S.C. § 112*

**Claims 6-8, 14-17, 22, 25, 30, 32, 40, 45, and 50-59** are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner asserts that "substantially inhibit" is unclear, and that one of ordinary skill in the art would not understand the metes and bounds of the word "substantially" to be able to envision the scope of the instant claims. Although Applicants disagree, solely in an effort to advance prosecution, claims 25 and 30 are amended to remove "substantially inhibit." Therefore, Applicants submit that these claims, and each of the claims dependent thereon, do particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claims 6, 7, 22, 40, 45, 50, 51, 57 and 58 are canceled, rendering the rejection of these claims moot.

In view of the foregoing amendment, Applicants request that the rejection of claims 8, 14-17, 25, 30, 32, 52-56 and 59 be withdrawn.

**Claims 6-8, 14-17, 22, 25, 30, 32, 40, 45, and 50-59** are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner alleges that the newly added limitation “wherein the antisense oligonucleotide does not substantially inhibit plasminogen” constitutes new matter. While Applicants disagree with the Examiner’s assertion that this limitation introduces new matter, in an effort to advance prosecution, the claims are amended such that they no longer recite “wherein the antisense oligonucleotide does not substantially inhibit plasminogen.” Applicants submit that the subject matter of the instantly claimed methods was adequately described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors were in possession of the claimed invention at the time the application was filed. Claims 6, 7, 22, 40, 45, 50, and 51 are canceled, rendering the rejection of these claims moot.

In addition to the foregoing rejection, **claims 6-8, 14-17, 22, 25, 30, 32, 40, 45, and 50-59** are rejected as allegedly lacking support over their entire scope. In particular, the Examiner contends that the specification does not provide a description of the genus of antisense oligonucleotides that inhibit apolipoprotein(a) without substantially inhibiting plasminogen, and further that the skilled artisan would not be able to envision such a genus of antisense oligonucleotides. Additionally, the Examiner asserts that the skilled artisan would not be able to envision which antisense oligonucleotides would inhibit apolipoprotein(a) by at least 10% without substantially inhibiting plasminogen without undue experimentation. Applicants respectfully disagree. However, for the purpose of advancing prosecution, the claims are amended such that they no longer recite “does not substantially inhibit plasminogen, and wherein said antisense oligonucleotide inhibits the expression of apolipoprotein(a) mRNA by at least 10%.” Applicants submit that the subject matter of the instantly claimed methods was adequately described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors were in possession of the claimed invention at the time the application was filed. As discussed above, claims 6, 7, 22, 40, 45, 50, and 51 are canceled, rendering the rejection of these claims moot.

In view of the foregoing amendment, Applicants request withdrawal of the rejection of claims 8, 14-17, 25, 30, 32, 52-56 and 59 under 35 U.S.C. § 112, first paragraph.

**Claims 30, 32, 45, 50-56, 58, and 59** are rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter that is not enabled by the specification. While, the Examiner acknowledges that the specification is enabling for a treatment method via intraperitoneal injection of an apolipoprotein(a) antisense oligonucleotide, the Examiner asserts that the specification is not enabling for the treatment of the broad scope of instantly recited diseases or disorders via any delivery means. Applicants respectfully disagree.

First, the Examiner contends that while the declaration pursuant to 37 C.F.R. 1.132 filed on 2/27/2006 teaches intraperitoneal injection of an antisense oligonucleotide, Applicants are not enable for the broad scope of any means of delivery. As stated in the Summary of Interview on page 6 of this paper, and in the Interview Summary prepared by the Examiner, Applicants do not need to specify a mode of administration to overcome the pending enablement rejection.

The Examiner further contends that, although Applicants have demonstrated a reduction in apolipoprotein(a) protein levels, Applicants are not enabled for the broad scope of instantly recited diseases or disorders. Solely in the interest of advancing prosecution, claim 30 is amended to recite “selecting a human having elevated lipoprotein(a) levels.” In the specification as filed, the second full paragraph of page 3 teaches that elevated plasma levels of lipoprotein(a) are caused by an increased expression of apolipoprotein(a). Accordingly, the specification as filed is enabling for treatment of a disease or condition treatable by the reduction of apolipoprotein(a), comprising selecting a human having elevated lipoprotein(a) levels.

For at least these reasons, Applicants submit that the specification fully enables one of ordinary skill in the art to make and use the claimed invention, and Applicants therefore request that the enablement rejection be withdrawn. Claims 45, 50, and 51 are canceled, rendering the rejection of these claims moot.

*35 U.S.C. 102(e) or 103(a)*

**Claims 6, 14, 16, 22, 25, 40, and 57** are rejected under 35 U.S.C. 102(e) as allegedly anticipated by, or in the alternative, under 35 U.S.C. 103(a) as obvious over Ben-David et al. The Examiner asserts that the antisense oligonucleotide taught by Ben-David et al. is fully complementary to a portion of SEQ ID NO: 4. Applicants respectfully disagree.

The antisense oligonucleotide taught by Ben-David et al. is fully complementary to

nucleotides 175-184 of instant SEQ ID NO: 4. The Examiner alleges that, because the antisense oligonucleotide of Ben-David et al. meets each of the structural limitations of the instant claims, and would therefore be expected to inhibit the expression of apolipoprotein(a) by at least 10%, the oligonucleotide would necessarily "not substantially inhibit plasminogen" as instantly claimed. Claim 25 as amended recites antisense oligonucleotides having at least 8 consecutive nucleobases of SEQ ID NO: 23. The sequence of Ben-David et al. does not meet the structural limitations of claim 25, or any claim depending therefrom. Furthermore, Ben-David et al. do not teach or suggest all of the limitations of amended claim 25, or the claims depending therefrom. Claims 6, 22, 40, and 57 have been canceled, rendering the rejection of these claims moot.

In view of the foregoing amendment and remarks, Applicants respectfully request that the rejection of claims 14, 16 and 25 be withdrawn.

### CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any issues remain or require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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